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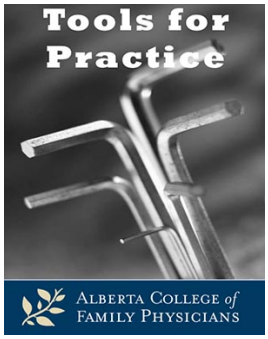

Is less more with isotretinoin and acne?

Clinical Question: What is the efficacy and tolerability of low-dose compared to conventional dose isotretinoin in the treatment of acne?

Bottom-line: Small randomized controlled trials (RCTs) and observational studies demonstrate low-dose (~20mg/day) isotretinoin improves acne similar to conventional dosing. Low-dose may reduce common side effects (chapped lips, dry skin, epistaxis) by 16-35% but may be associated with increased relapse rates, particularly with severe acne and/or possibly impacted by lower total accumulated dose.

Evidence:

- Three RCTs compare conventional to low dosing:
  - 60 moderate acne patients, low (0.25-0.4 mg/kg/day) or "conventional" dosing (0.5-0.7 mg/kg/day) for 24 weeks.[1] Low-dose demonstrated:
    - Equivalent efficacy (acne grading and lesion counts).
    - Increased patient satisfaction (76% very satisfied versus 31%).
    - Higher (non-significant) one year relapse rate: 18% versus 13%.
  - 150 severe treatment resistant nodulocystic acne patients, 0.1 mg/kg/day, 0.5 mg/kg/day or 1.0 mg/kg/day for 20 weeks.[2]
    - Equivalent improvement with all doses.
    - Eighteen month relapse rates, from lowest-highest doses: 42%, 20%, and 10%.
  - Both studies reported 16-35% fewer common side effects (chapped lips, dry skin, and epistaxis) with lower doses.[1,2]
  - 120 mild-severe acne patients, high (1 mg/kg/day) or low-dose (20 mg/day) alternating days for 16 weeks.[3] Low-dose:
    - Decrease in acne load 81% versus 95%.
    - Fewer side effects.
- Large prospective study (638 moderate acne patients, 20 mg/day for 24 weeks) reported "good results" in ~94% of patients, decreased incidence of side effects and 5% relapse at four years.[4]

- Smaller observational studies of ~20mg/day support these findings.[5,6,7] Two report improved outcomes with a 120 mg/kg total cumulative dose.[5,7]

Context:

- FDA approved isotretinoin in 1982 for the treatment of severe acne in patients ≥12 years old. The recommended dosage is 0.5-1 mg/kg divided into two doses daily for 4-5 months.[8]
- Many lower-dose studies do not reach a similar total accumulated dose as the higher dose treatment arm(s), which may partly explain higher relapse rates.[1-3]
- Recommended laboratory monitoring includes triglycerides, cholesterol, transaminase, and complete blood counts.[9,10]
- Although there are reports of mood changes, suicidal ideation and suicide, no causal relationship is proven.[9,10]
- Isotretinoin is teratogenic and pregnancy must be prevented one month before, during, and after treatment.[9,10]

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Disclosure:
Authors do not have any conflicts to disclose.

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